# MATERNAL SMOKING, POLYMORPHISMS IN *CYP1A1*, *CYP2E1*, *EPHX1*, *NAT2*, *NQO1*, AND CHILDHOOD ACUTE LEUKEMIA

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**Background and Aims:** Antenatal passive exposure to tobacco smoke could influence early steps of leukemogenesis. This study aimed to explore the effect of maternal smoking during pregnancy on childhood acute leukemia (AL), accounting for genetic polymorphisms that modulate metabolite production.
**Methods:** Data are drawn from the national population-based study ESCALE, which included 764 AL and 1681 controls in 2003-2004. Mothers of cases and controls were interviewed by telephone on their tobacco consumption during pregnancy, using a standardized questionnaire. A sub-sample of 493 cases (433 lymphoblastic (ALL) and 51 myeloblastic (AML)) and 549 controls, with European ancestry from at least 2 grandparents, was genotyped on Illumina high throughput platforms. Genotype imputation was used to complete the data for untyped polymorphisms. Candidate alleles were *CYP1A1*2A/2B* (rs4646903), *CYP2E1*5* (rs2031920, rs3813867), *NQO1*2* (rs1800566), *NAT2*5* (rs1801280) and *EPHX1* polymorphisms in exons 3 (rs1051740) and 4 (rs2234922). Logistic regression models were adjusted on the gender*age quota sampling variable used for the selection of controls, birth order, breastfeeding and socioeconomic parental situation. Gene-environment interactions were also assessed by case-only analyses.
**Results:** ALL and AML were associated neither with maternal smoking during pregnancy, nor with candidate polymorphisms in *CYP1A1*, *CYP2E1, EPHX1* and *NQO1*. The presence of two slow *NAT2*5* alleles was significantly associated with ALL (OR=1.7 [1.2-2.6]). Analyses suggested an interaction borderline of significance between the slow *EPHX1* phenotype (rs1051740 CT or CC, rs2234922 AA) and the slow *NAT2* phenotype (rs1801280 CC). There was no interaction between any of the polymorphisms under study and maternal smoking.
**Conclusions:** The ESCALE study did not evidence the interaction between maternal smoking and *CYP1A1*2A/2B* suggested previously (Clavel et al., 2005). The association with NAT2 slow phenotype is compatible with the only previous study reporting on this phenotype in childhood ALL (Krajinovic et al., 2000). The interaction *EPHX1-NAT2* needs replication.

**References:**
Clavel J, Bellec S, Rebouissou S, Menegaux F, Feunteun J, Bonaiti-Pellie C, Baruchel A, Kebaili K, Lambilliotte A, Leverger G et al: Childhood leukaemia, polymorphisms of metabolism enzyme genes, and interactions with maternal tobacco, coffee and alcohol consumption during pregnancy. Eur J Cancer Prev 2005, 14(6):531-40.
Krajinovic M, Richer C, Sinnett H, Labuda D, Sinnett D: Genetic polymorphisms of N-acetyltransferases 1 and 2 and gene-gene interaction in the susceptibility to childhood acute lymphoblastic leukemia. Cancer Epidemiol Biomarkers Prev 2000, 9(6):557-62.